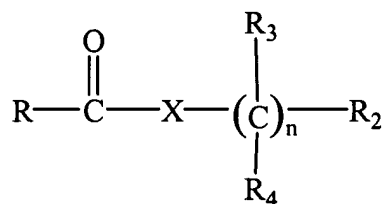


Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application.

Listing of the Claims:

Claim 1 (currently amended): A method of ameliorating cough in a subject comprising the local administration to the upper respiratory airways of [a] the subject in need of ~~such treatment of a cannabinoid compound~~ CB1 cannabinoid receptor agonist of formula I:



wherein X is N-R<sub>1</sub> [[N-R1]] or O;

R is a saturated or unsaturated, chiral or achiral, cyclic or acyclic, substituted or unsubstituted hydrocarbyl group, wherein the hydrocarbyl group has 11 to 29 carbon atoms;

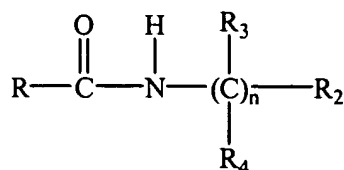
R<sub>1</sub>, R<sub>3</sub> and R<sub>4</sub> [[R1 , R3 and R4]] are selected independently from hydrogen, alkyl (C1-4), alkenyl (C2-4), alkynyl (C2-4), cycloalkyl (C3-6), or a hydroxyalkyl group with from 2 to 4 carbon atoms;

R<sub>2</sub> [[R2]] is OH or O-CO-alkyl, where the alkyl group has from 1 to 4 carbon atoms; and

n is selected from 2 to 4.

Claims 2-4 (canceled).

Claim 5 (currently amended): A method of ameliorating cough comprising the local administration to the upper respiratory airways of a subject in need of such treatment of a ~~cannabinoid compound~~ CB1 cannabinoid receptor agonist of formula II:



wherein R is a saturated or unsaturated, substituted or unsubstituted hydrocarbyl group with from 15 to 29 carbon atoms;

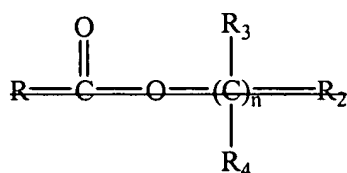
R<sub>3</sub> and R<sub>4</sub> [R3 and R4] are selected independently from hydrogen, alkyl (C1-4), alkenyl (C2-4), alkynyl (C2-4), cycloalkyl (C3-6), or hydroxyalkyl group with from 2 to 4 carbon atoms;

R<sub>2</sub> [R2] is OH or O-CO-alkyl, where the alkyl group has from 1 to 4 carbon atoms; and

n is an integer selected from 2 to 4.

Claims 6 -7 (canceled).

Claim 8 (currently amended): A method of ameliorating cough comprising the local administration to the upper respiratory airways of a subject in need of such treatment of 2-arachidonylglycerol. ~~of a cannabinoid compound of formula III:~~



~~wherein R is a saturated or unsaturated; substituted or unsubstituted hydrocarbyl group with from 15 to 29 carbon atoms;~~

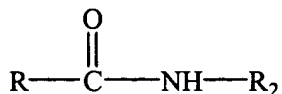
~~R<sub>3</sub> and R<sub>4</sub> [R3 and R4] are selected independently from hydrogen, alkyl (C1-4), alkenyl (C2-4), alkynyl (C2-4), cycloalkyl (C3-6), or hydroxyalkyl group with from 2 to 4 carbon atoms;~~

~~R<sub>2</sub> [R2] is OH or O-CO-alkyl, where the alkyl group of O-CO-alkyl has from 1 to 4 carbon atoms; and~~

~~n is selected from 2 to 4.~~

1 Claim 9 (canceled).

1 Claim 10 (currently amended): A method of ameliorating cough in a subject  
2 comprising the local administration to the upper respiratory airways of the [a] subject or the  
3 systemic administration to the subject ~~in need of such treatment~~ of an inhibitor of endogenous  
4 cannabinoid inactivation of formula IV:

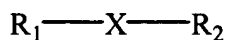


6 wherein R is a polyunsaturated, substituted or unsubstituted hydrocarbyl group,  
7 wherein the hydrocarbyl group has from 18 to 22 carbon atoms;

8 R<sub>2</sub> [[R2]] is selected independently from substituted or unsubstituted cycloalkyl  
9 (C3-6) group and substituted or unsubstituted phenyl group.

1 Claim 11 (original): The method of claim 10, wherein the phenyl group is  
2 selected from the group consisting of p-hydroxyphenyl and p-hydroxy-o-methyl-phenyl.

1 Claim 12 (currently amended): A method of ameliorating cough comprising the  
2 local administration to the upper respiratory airways of a subject or the systemic administration  
3 to subject in need of such treatment of an inhibitor of endogenous cannabinoid inactivation of  
4 formula V:



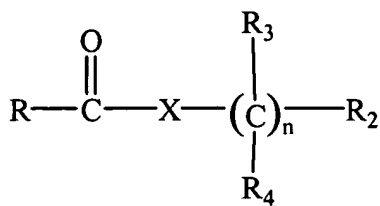
6 wherein [[R1]] R<sub>1</sub> is a saturated or polyunsaturated, substituted or unsubstituted  
7 hydrocarbyl group, wherein the hydrocarbyl group has from 6 to 22 carbon atoms;

8 X is -C=O or SO<sub>2</sub>-; and

9 R<sub>2</sub> [[R2]] is a halogen or a halogen-substituted methyl group.

10 Claim 13 (currently amended): The method of claim 1, wherein the ~~cause of the~~  
11 cough is selected from the group consisting of a can be persisting dry cough resulting from  
12 airway irritation and/or infection, an angiotensin converting enzyme (ACE) ~~inhibitors-induced~~  
13 inhibitor-induced cough, and a cancer-induced cough.

Claim 14 (currently amended): The method of claim 10, wherein the method further comprises administration of a CB1 cannabinoid receptor agonist compound of formulae I, ~~II or III~~, formula I:



wherein X is N-R<sub>1</sub> or O;

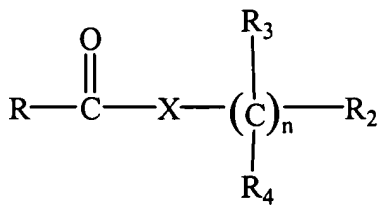
R is a saturated or unsaturated, chiral or achiral, cyclic or acyclic, substituted or unsubstituted hydrocarbyl group, wherein the hydrocarbyl group has 11 to 29 carbon atoms;

R<sub>1</sub>, R<sub>3</sub> and R<sub>4</sub> are each selected independently from hydrogen, alkyl (C1-4), alkenyl (C2-4), alkynyl (C2-4), cycloalkyl (C3-6), or a hydroxyalkyl group with from 2 to 4 carbon atoms;

R<sub>2</sub> is OH or O-CO-alkyl, where the alkyl group has from 1 to 4 carbon atoms; and n is an integer from 2 to 4.

~~or any combination thereof.~~

Claim 15 (currently amended): The method of claim 11, wherein the method further comprises administration of a CB1 cannabinoid receptor agonist compound of formula I:



wherein X is N-R<sub>1</sub> or O;

R is a saturated or unsaturated, chiral or achiral, cyclic or acyclic, substituted or unsubstituted hydrocarbyl group, wherein the hydrocarbyl group has 11 to 29 carbon atoms;

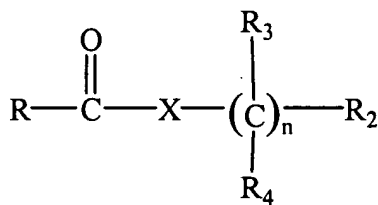
R<sub>1</sub>, R<sub>3</sub> and R<sub>4</sub> are each selected independently from hydrogen, alkyl (C1-4), alkenyl (C2-4), alkynyl (C2-4), cycloalkyl (C3-6), or a hydroxyalkyl group with from 2 to 4 carbon atoms;

R<sub>2</sub> is OH or O-CO-alkyl, where the alkyl group has from 1 to 4 carbon atoms; and

n is an integer from from 2 to 4.

formulae I, II, III, or any combination thereof.

Claim 16 (currently amended): A method of ameliorating cough comprising the local administration of a CB1 cannabinoid receptor agonist of formula I ~~cannabinoid compound of formulae I, II, III, or any combination thereof~~, to the upper respiratory airways of a ~~patients~~ patient in need of such treatment and whose vagal control of airway responsiveness is functional, wherein the formula I is:



wherein X is N-R<sub>1</sub> or O;

R is a saturated or unsaturated, chiral or achiral, cyclic or acyclic, substituted or unsubstituted hydrocarbyl group, wherein the hydrocarbyl group has 11 to 29 carbon atoms;

R<sub>1</sub>, R<sub>3</sub> and R<sub>4</sub> are selected independently from hydrogen, alkyl (C1-4), alkenyl (C2-4), alkynyl (C2-4), cycloalkyl (C3-6), or a hydroxyalkyl group with from 2 to 4 carbon atoms;

R<sub>2</sub> is OH or O-CO-alkyl, where the alkyl group has from 1 to 4 carbon atoms; and

n is an integer from 2 to 4.

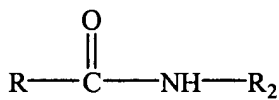
Claims 17-18 (canceled).

1 Claim 19 (currently amended): The method of claim 1 wherein the agonist a  
2 ~~cannabinoid of formulae~~ formula I is selected from the group consisting of  
3 arachidonylethanolamide (anandamide), (R)-(+)-arachidonyl-1'-hydroxy-2'-propylamide, cis-7,  
4 10, 13, 16-docosatetraenoylethanolamide, homo-delta-linoleyethanolamide, and N-propyl-  
5 arachidonylethanolamide.

1 Claim 20 (currently amended): The method of claim 10 wherein the [a]  
2 cannabinoid inactivation inhibitor of formula IV is 4-(hydroxyphenyl)-arachidonamide.

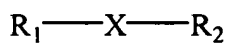
1 Claims 21-22 (canceled).

1 Claim 23 (currently amended): The method of claim 16, [[22]] wherein the  
2 method further comprises local or systemic administration of a pharmaceutical composition  
3 comprising a cannabinoid inactivation inhibitor of [[formula IV, V]] formula IV or formula V, or  
4 any combination thereof, wherein the formula IV is



5  
6 wherein R is a polyunsaturated, substituted or unsubstituted hydrocarbyl group,  
7 wherein the hydrocarbyl group has from 18 to 22 carbon atoms; R<sub>2</sub> is selected independently  
8 from substituted or unsubstituted cycloalkyl (C3-6) group and substituted or unsubstituted  
9 phenyl group;

10 and the formula V is



11  
12 wherein R<sub>1</sub> is a saturated or polyunsaturated, substituted or unsubstituted  
13 hydrocarbyl group, wherein the hydrocarbyl group has from 6 to 22 carbon atoms;

14 X is -C=O or SO<sub>2</sub>-; and

15 R<sub>2</sub> is a halogen or a halogen-substituted methyl group.

1 Claim 24 (canceled).

1 Claim 25 (currently amended): The method of claim 16 ~~[[22]]~~ wherein the  
2 pharmaceutical composition is formulated for local delivery.

1 Claim 26 (currently amended): The method of claim 25 wherein the ~~formulation~~  
2 ~~for~~ local delivery is by aerosol.

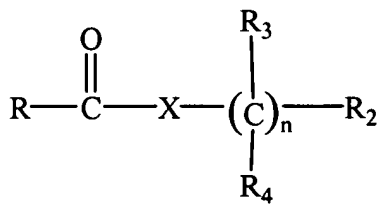
1 Claim 27 (original): The method of claim 23 wherein the pharmaceutical  
2 composition is formulated for local delivery.

1 Claim 28 (currently amended): The method of claim 27 wherein the ~~formulation~~  
2 ~~for~~ local delivery is by aerosol.

1 Claim 29 (original): The method of claim 23 wherein the pharmaceutical  
2 composition is formulated for systemic delivery.

1 Claim 30 (currently amended) The method of claim 29 wherein the ~~formulation~~  
2 ~~for~~ systemic delivery is by oral administration or intravenous administration.

1 Claim 31 (Currently amended): A pharmaceutical composition comprising a  
2 locally acting cannabinoid of formulae I, II, III, ~~or any combination thereof~~, wherein the  
3 cannabinoid ameliorates cough and produces, at most, clinically insignificant dysphoric side  
4 effects, and wherein formula I is:



6 wherein X is N-R<sub>1</sub> or O;

7 R is a saturated or unsaturated, chiral or achiral, cyclic or acyclic, substituted or  
8 unsubstituted hydrocarbyl group, wherein the hydrocarbyl group has 11 to 29 carbon atoms;

R<sub>1</sub>, R<sub>3</sub> and R<sub>4</sub> are selected independently from hydrogen, alkyl (C1-4), alkenyl (C2-4), alkynyl (C2-4), cycloalkyl (C3-6), or a hydroxyalkyl group with from 2 to 4 carbon atoms;

R<sub>2</sub> is OH or O-CO-alkyl, where the alkyl group has from 1 to 4 carbon atoms; and

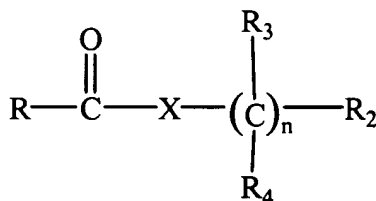
n is an integer from 2 to 4;

and wherein the cannabinoid is formulated for localized delivery to the upper airways.

Claim 32 (original): The pharmaceutical composition of claim 31 further comprising a pharmaceutically acceptable excipient.

Claims 33-36 (Canceled).

Claim 37 (currently amended): A method of ameliorating cough in a subject comprising the local administration to the upper respiratory airways of [a] the subject in need of such treatment of a cannabinoid compound CB1 cannabinoid receptor agonist of formula I:



where R is a saturated or unsaturated, chiral or achiral, cyclic or acyclic, substituted or unsubstituted hydrocarbyl group, wherein the hydrocarbyl group has with from 11 to 29 carbon atoms; and excluding aryl and methylene groups in said R optionally substituted with from 1 to 6 O or S atoms;

X is NH and R<sub>2</sub> is OH [[X is NR<sub>1</sub> or O]]

R<sub>1</sub>, R<sub>3</sub> and R<sub>4</sub> [[R<sub>1</sub>, R<sub>3</sub> and R<sub>4</sub>]] are selected independently from the group consisting of hydrogen, alkyl (C1-4), alkenyl (C2-4), alkynyl (C2-4), cycloalkyl (C3-6), and a [[or]] hydroxyalkyl group with from 2 to 4 carbon atoms;



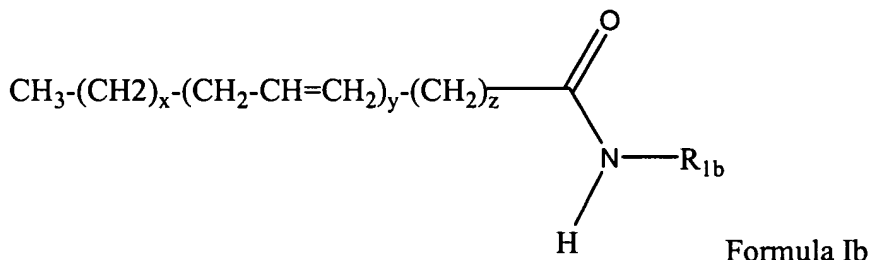
- 13  ~~$R_2$  [[R2]] is OH or O-CO-alkyl, where the alkyl group has from 1 to 4 carbon atoms; and~~  
14 ~~n is selected from 2 to 4~~  
15 ~~and wherein  $R_2$  and X are joined together to form a heterocyclic ring.~~

1 Claim 38 (canceled).

1 Claim 39 (currently amended): The method of claim [[38]] 37 where the  
2 heterocyclic ring structure is a selected from 2-oxazolidinone, morpholine or oxazepine ring.  
3

Claims 40-42 (canceled).

Claim 43 (new): The method of claim 1, wherein the compound has the formula:



wherein  $R_{1b}$  is  $(\text{CH}_2)_p-(\text{CH}_2)_q-(\text{CH}_2)_r\text{-OH}$ , wherein p, q and r are each an integer of from 1 to 4; provided that  $p+q+r$  are less than or equal to 4, x is an integer of from 0 to 18, y is an integer of from 0 to 8, and z is an integer of from 0 to 18.

Claim 44 (new): The method of claim 1, wherein  $R_1$  and  $R_3$  are each hydrogen, and  $R_2$  is hydroxy and n is 2.

Claim 45 (new): The method of claim 1, wherein R is an acyclic and unsubstituted hydrocarbyl group.

Claim 46 (new): The method of claim 5, wherein R is an acyclic and unsubstituted hydrocarbyl group.

Appl. No. 09/864,920

PATENT

Amdt. dated April 19, 2004

Reply to Office Action of on December 18, 2003

Claim 47 (new): The method of claim 1, wherein the agonist is selective for the CB1 cannabinoid receptor over the CB2 cannabinoid receptor.